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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,895	12/28/2001	Daniel S. Sem	P-TB 5072	1917

41552 7590 05/04/2005

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EXAMINER	
ZHOU, SHUBO	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,895	SEM ET AL.	
	Examiner	Art Unit	
	Shubo (Joe) Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-10,15-17 and 26-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14,18-25 and 29-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/8/02, 9/15/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Amendments

Applicants' election of Group II (claims 11-32) and the species of Hidden Markov Model in the communication filed 2/9/05, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Accordingly, claims 1-32 are currently pending and claims 11-14, 18-25, and 29-32 are under consideration. Claims 1-10, 15-17, and 26-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention (1-10) or species (15-17 and 26-28), there being no allowable generic or linking claim.

The preliminary amendments filed 10/23/03 and 6/1/04 are acknowledged and entered.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence(s) of the specification or in an application data sheet by identifying the prior application by application number (37 CFR 1.78(a)(2) and (a)(5)). If the prior application is a non-provisional application, the specific reference must also include the relationship (i.e., continuation, divisional, or continuation-in-

part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

It is noted that the amendment filed 10/23/03 amended the first paragraph of the specification to claim priority to prior applications 60/367,371, filed 12/29/2000, and non-provisional application 09/753,020, filed 12/29/2000. However, the relationship between application 09/753,020 and the instant application is not specified. While the ADS filed 12/28/01 refers to the application, it again does not specify a relationship.

Further, the current status of application 09/753,020 should be updated.

Information Disclosure Statement

The Information Disclosure Statements filed 4/8/02 and 9/15/03, respectively, have been entered and considered. Initialed copies of the form PTO-1449 are enclosed with this action.

Specification

The specification is objected to because of the following:

The title of the invention is not descriptive. The elected invention is drawn to a method for identifying a member of a pharmacofamily, whereas the title is directed to methods for predicting functional and structural properties of polypeptides using sequence models. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

The numbering of the Tables in the specification is confusing. It seems that there are Tables 1-18 and 20, but no Table 19.

The disclosure is objected to also because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification at page 100. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP ' 608.01.

The specification on page 5 refers to Figure 3 and parts thereof, whereas the drawings filed 12/28/01 do not have Figure 3, but instead Figures 3A through 3H.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-14, 18-25, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (IDS document: PNAS, Vol. 97, pages 3965-3970) in view of Vernier et al. (TiPS, Vol. 16, pages 375-381, 1995) and Felsenstein et al. (Mol. Biolo. Evol. Vol. 13, pages 93-104, 1996).

The claims are drawn to method for identifying a member of a pharmacofamily comprising a sequence of a polypeptide to a sequence model and determining a relationship between the sequence and the sequence model.

Johnson et al. disclose a method of identifying a member of bacterial receptor families, LacI/RbsB and SubI. The method comprises performing multiple alignments of known members of a receptor family in Swiss-Prot database to built a model (sequence alignment) with hidden Markov modeling, and the model is then compared to a particular receptor protein sequence. If the sequence has binding site identity > 50% or similarity > 65%, the sequence is added to the family. The entire process of multiple alignments is performed by adding new sequences gradually into an alignment of seed sequences by different rounds of hidden Markov modeling. See page 3966, left column "Methods."

Johnson et al. do not explicitly teach of identifying a member of a pharmacofamily.

Johnson et al. state that their methods "are applicable to receptors as well as enzymes" and "will be straightforward to add to large-scale automated annotation algorithms used for new

genomic data and will be particularly useful in assigning residue-specific function within other families of receptors."

Felsenstein et al. apply hidden Markov model in analyzing sequences from different organisms such as rat and human (see the data example on page 101).

Given the motivation of Johnson et al. to use their hidden Markov sequence modeling hidden Markov model for other receptors and enzymes and that the method of hidden Markov model has been used to analyze sequences of proteins from human, one of ordinary skill in the art would have been motivated to use the method of Johnson et al. to analyze sequences from human.

Further, it would have been obvious to one of ordinary skill in the art that proteins, especially receptors, were frequently drugs or drug targets, which involves various families of proteins. For example, Vernier et al. disclose that the human bioamine receptor family proteins are pharmacologically significant and the "receptors are classified on the basis of drug activity." See page 375, left column. It would also have been obvious to one of ordinary skill in the art that the method of Johnson et al. would apply to any protein families including those who are drug or drug targets of pharmacofamilies since Johnson et al. do not specify any limitations.

Thus, one of ordinary skill in the art would have been motivated to modify the method of Johnson et al. to apply their method to identify new members for a drug or drug target of pharmacofamilies.

As to claims 12-13, while Johnson et al. do not explicitly disclose that the sequence model comprises nucleic acid sequence, it would have been obvious to one of ordinary skill in the art that the sequence model could comprise either amino acid sequence or nucleic acid

sequence encoding such amino acid sequence given that the genetic code for nucleic acid sequences encoding an amino acid sequence would have been well known in the art. Further, since, as set forth above, Johnson et al. motivate using their methods for large-scale automated annotation for new genomic data, and it would be obvious that such genomic data are nucleic acid sequences, using nucleic acid sequences instead of amino acid sequences in the sequence modeling would have been obvious to one of ordinary skill in the art at the time the invention was made.

As to claim 14, the model used by Johnson et al. is HMM (hidden Markov model). See page 3966, left column.

As to claims 18-19, the sequence model in the method of Johnson et al. includes a set of polypeptide sequences of different members of the bacterial receptor family that are multiple-aligned by ALIGNMENTBUILDER. Further, the method includes adding new member to the family and repeating multiple times. See page 3966, left column, especially the 2nd and 3rd paragraphs.

As to claims 20-21, the binding site sequence alignments in the method of Johnson et al. is a subset of the amino acids of the members of the receptor families. Johnson et al. disclose that the binding site residues for each structure were defined as those with a side chain heavy atom < 4.5 Angstrom from the ligand. This reads on the recitation in the claims that the amino acid sequences have one or more atoms within a selected distance from a bound ligand. See page 3966, left column.

As to claims 22-25 and 29-32, which recite two differential sequence models were used, Johnson et al. disclose that for the sequence modeling of LacI/RbsB family, the initial alignments

were done by the Homology module of a modeling program InsightII, and the alignment modeling continues by adding new members by ALIGNMENTBUILDER, a hidden Markov model. With regard to the initial sequences in the multiple alignments, they've actually undergone comparisons of the sequences with other sequences in the eventual converged alignment by two different models, one the Homology module of InsightII and the other the ALIGNMENTBUILDER, a hidden Markov model. These two models are interpreted as being differential models as recited in the claims. See page 3966, left column. For other limitations of claims 23-25 and 29-32, see that which is applied above to claims 12-14 and 18-21.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are

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Shubo (Joe) Zhou, Ph.D.

Patent Examiner

Ardin H. Marschel 5/2/05

ARDIN H. MARSCHEL
PRIMARY EXAMINER